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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,845	11/14/2001	Karen A. McDonald	023070-114510US	7257

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EXAMINER

KALLIS, RUSSELL

ART UNIT PAPER NUMBER

1638

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/992,845

Applicant(s)

MCDONALD ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-13 and 15-25 is/are pending in the application.
- 4a) Of the above claim(s) 7-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-6 and 15-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Claims 2, 3 and 14 are cancelled. New claims 18-25 are added. Claims 7-13 are withdrawn. Claims 1, 4-6 and 15-25 are examined. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 25 is objected to because of the following informalities: The claim is improperly dependent upon non-elected Claim 11. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1, 4-6, and 15-17 remain and new Claims 18-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of semi-continuous growth of rice suspension cells transformed with the *Ramy3D* promoter operably linked to a human α_1 -antitrypsin, does not reasonably provide enablement for a method of semi-continuous growth of any plant cell suspension culture expressing any protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/18/2004.

Applicant's arguments filed 7/19/2004 have been considered but are not deemed persuasive.

Applicant asserts that one of skill in the art would know how to avoid inoperative embodiments (page 7 specification, lines 1-6). See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

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Applicant asserts that the previous office action alleged that the increases in medium pH were due to the ionic nature of the recombinant protein produced (response page 8). The office action did not allege that the pH increase observed in Applicant's invention was due to the secretion of human α_1 -antitrypsin into the growth medium. The enablement rejection was not directed to the recombinant expression of human α_1 -antitrypsin in transformed rice cells, but rather to the vast number of inoperative embodiments resulting from unknown cell types and non-exemplified proteins that fall within the broad scope of the claims.

Applicants' assertions that an increase in recombinant protein expression levels are coincidental with an increase in medium pH (response page 9, lines 4-6) and the result of cell growth are in contrast with the teachings on page 5, lines 7-11 of the specification, which state that several variables will influence the rise in pH, notably culture conditions, cell type and protein produced. Further, although Applicant states that attached Figure 1 of the declaration filed 7/22/2004 provides evidence that pH will increase in the absence of recombinant protein production. However, attached Figure 1 of Applicants' declaration does indicate that total protein in the induction medium did increase and was correlated with a rise in pH, and hence it is not clear that protein levels, recombinant or otherwise do not influence medium pH. Applicant has not enabled the invention for the broad scope.

Claim Rejections - 35 USC § 103

Claims 1, 4-6 and 15-17 remain and new Claims 18-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terashima M. *et al.* (Appl. Microbiol. Biotechnol., 1999; Vol. 52 pages 516-523) in view of Fischer U. *et al.* (Plant Cell, Tissue and Organ Culture, 1994, Vol. 38; pages 123-134) and Applicant's admission. This rejection is maintained for the reasons of

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record set forth in the Official action mailed 2/18/2004. Applicant's arguments filed 7/19/2004 have been considered but are not deemed persuasive.

Applicant asserts that the Examiner was reading out of context the paragraph that begins "One of skill in the art will recognize. . . " on page 5 of the specification and further asserts that the correlation between a pH increase in induction medium and recombinant protein levels was discovered by the inventors and not known to those of skill in the art prior to the filing of their application (response page 11). Applicant has not indicated which paragraph is providing the context. Nonetheless, this is not the case because the paragraph does not address any particular context and states broadly that one of skill in the art will recognize that the optimal pH value for protein production will vary depending upon the culture conditions, the type of cells, and the protein produced. Clearly this paragraph does not need context and stands alone as a statement of the level of the art, and thus provides motivation to monitor pH.

Applicant asserts that the Examiner has failed to provide a reasonable expectation of success in practicing the invention and to provide a motivation to combine the references (response page 10, 2nd full paragraph) and further asserts that Terashima does not teach reuse of the cells (response page 10 3rd full paragraph). Terashima provides a reasonable expectation of success by teaching a method of continuous expression of human α_1 -antitrypsin in transformed rice cells, and by suggesting optimization of culture conditions and by suggesting repeating the growth-production cycle shown in figure 5 for increased yield of protein on page 521, column 2, 3rd paragraph lines 9-13. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where

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there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation to combine the references is provided by Terashima by suggesting optimization of culture conditions and by suggesting repeating the growth-production cycle shown in figure 5 for increased yield of protein on page 521, column 2, 3rd paragraph lines 9-13, by Fischer's teachings of semi-continuous culturing method, in view of Applicant's admission that it is known in the art that the pH value for optimal protein production will vary and thus provides motivation to monitor pH; and in view of Applicant's teaching in the specification that promoters of Claim 22 are known in the art and wherein isolating the recombinant protein from the induction medium of Claim 20 is an obvious method step.

Applicant asserts that the Terashima and Fisher references do not provide motivation for measurement of pH to determine protein expression levels or to improve their production methods levels (response page 11 2nd paragraph). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation to combine the references is provided by Terashima by suggesting optimization of culture conditions and by suggesting repeating the growth-production cycle shown in figure 5 for increased yield of protein on page

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521, column 2, 3rd paragraph lines 9-13, by Fischer's teachings of semi-continuous culturing method, in view of Applicant's admission that it is known in the art that the pH value for optimal protein production will vary and thus provides motivation to monitor pH; and in view of Applicant's teaching in the specification that promoters of Claim 22 are known in the art and wherein isolating the recombinant protein from the induction medium of Claim 20 is an obvious method step.

Applicant further asserts that any admission in the application perceived by the Examiner is in error and cannot be used to find motivation for measurement of pH levels to determine protein expression levels (response last 2 lines of page 11 to page 12). In response to applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which applicant relies (i.e., changing an induction medium with a growth medium after the pH of the induction medium changes and says nothing about optimizing protein levels) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No Claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
November 8, 2004



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